

What is claimed is:

1. An animal having a heterologous nucleic acid sequence replacing an allele of an *atonal*-associated nucleic acid sequence under conditions wherein said heterologous sequence inactivates said allele.
2. The animal of claim 1 wherein said heterologous nucleic acid sequence is expressed under the control of an *atonal*-associated regulatory sequence.
3. The animal of claim 1 wherein both *atonal*-associated alleles are replaced.
4. The animal of claim 3 wherein said heterologous nucleic acid sequences are nonidentical.
5. The animal of claim 3 wherein said animal has a detectable condition.
6. The animal of claim 5 wherein said detectable condition is selected from the group consisting of loss of hair cells, cerebellar granule neuron deficiencies, hearing impairment, an imbalance disorder, joint disease, osteoarthritis and abnormal proliferation of cells.
7. The animal of claim 1 or 3 wherein said heterologous nucleic acid sequence is a reporter sequence.
8. The animal of claim 1 or 3, wherein said *atonal*-associated allele is replaced with an *atonal*-associated nucleic acid sequence under the control of regulatable promoter sequence.
9. The animal of claim 1 or 3, wherein said *atonal*-associated allele is replaced with an *atonal*-associated nucleic acid sequence under the control of a tissue-specific promoter sequence.

10. The animal of claim 1 or 3 wherein said animal is selected from the group consisting of a mouse, *Drosophila*, zebrafish, frog, rat, hamster and guinea pig.

11. A method for screening for a compound in an animal wherein said compound affects expression of an *atonal*-associated nucleic acid sequence comprising:

delivering said compound to said animal, wherein said animal has at least one allele of an *atonal*-associated nucleic acid sequence inactivated by insertion of a heterologous nucleic acid sequence, wherein said heterologous nucleic acid sequence is under control of an *atonal*-associated regulatory sequence; and

monitoring for a change in said expression of said *atonal*-associated nucleic acid sequence.

12. The method of claim 11 wherein said compound affects expression of an *atonal*-associated nucleic acid sequence.

13. The method of claim 11 wherein said compound affects a detectable condition in an animal.

14. The method of claim 11, wherein said heterologous nucleic acid sequence is a reporter sequence.

15. A method for screening for a compound in an animal, wherein said compound affects a detectable condition in said animal, comprising:

delivering said compound to said animal wherein at least one allele of an *atonal*-associated nucleic acid sequence in said animal is inactivated by insertion of a heterologous nucleic acid sequence, wherein said heterologous nucleic acid sequence is under the control of an *atonal*-associated regulatory sequence, and

monitoring said animal for a change in the detectable condition.

16. The method of claim 11 or 15 wherein said compound affects said detectable condition.

17. The method of claim 15 wherein said compound affects expression of said heterologous nucleic acid sequence.

18. A method of treating an animal with a deficiency in cerebellar granule neurons or their precursors comprising delivery of a therapeutically effective amount of an *atonal*-associated amino acid sequence or nucleic acid sequence to a cell of said animal.

19. A method of promoting mechanoreceptive cell growth in an animal, comprising delivering a therapeutically effective amount of an *atonal*-associated amino acid sequence or nucleic acid sequence to a cell of said animal.

20. A method of generating hair cells comprising delivering a therapeutically effective amount of an *atonal*-associated amino acid sequence or nucleic acid sequence to a cell of said animal.

21. A method of treating an animal for hearing impairment, comprising delivering a therapeutically effective amount of an *atonal*-associated amino acid sequence or nucleic acid sequence to a cell of said animal.

22. A method of treating an animal for an imbalance disorder, comprising delivering a therapeutically effective amount of an *atonal*-associated amino acid sequence or nucleic acid sequence to a cell of said animal.

23. A method of treating an animal for a joint disease comprising delivering a therapeutically effective amount of an *atonal*-associated amino acid sequence or nucleic acid sequence to a cell of said animal.
24. A method of treating an animal for an abnormal proliferation of cells comprising
5 delivering a therapeutically effective amount of an *atonal*-associated amino acid sequence or nucleic acid sequence to a cell of said animal.
25. A method of treating an animal for an abnormal proliferation of cells comprising altering *atonal*-associated nucleic acid sequence or amino acid sequence levels in a cell.
- 10 26. A method of treating an animal for a disease that is a result of loss of functional *atonal*-associated nucleic acid or amino acid sequence comprising delivering a therapeutically effective amount of an *atonal*-associated amino acid sequence or nucleic acid sequence to a cell of said animal.
27. The method of claim 18, 19, 20, 21, 22, 23, 24, 25 or 26, wherein said amino acid
15 sequence or nucleic acid sequence is delivered by a delivery vehicle.
28. The method of claim 18, 19, 20, 21, 22, 23, 24, 25 or 26, wherein said amino acid sequence or nucleic acid sequence is delivered by a delivery vehicle, and wherein said delivery vehicle is selected from the group consisting of an adenoviral vector, a retroviral vector, an adeno-associated viral vector, a plasmid, a
20 liposome, a nucleic acid, a peptide, a lipid, a carbohydrate and a combination thereof.
29. The method of claim 18, 19, 20, 21, 22, 23, 24, 25 or 26, wherein said amino acid sequence or nucleic acid sequence is delivered by a delivery vehicle, wherein said

delivery vehicle is selected from the group consisting of a viral vector or a non-viral vector.

30. The method of claim 18, 19, 20, 21, 22, 23, 24, 25 or 26, wherein said amino acid sequence or nucleic acid sequence is delivered by a delivery vehicle, and wherein

5 said delivery vehicle is a cell.

31. The method of claim 18, 19, 20, 21, 22, 23, 24, 25 or 26, wherein said *atonal*-associated amino acid sequence or nucleic acid sequence is Math1.

32. The method of claim 18, 19, 20, 21, 22, 23, 24, 25 or 26, wherein said *atonal*-associated amino acid sequence or nucleic acid sequence is Hath1.

10 33. The method of claim 18, 19, 20, 21, 22, 23, 24, 25 or 26, wherein said cell contains an alteration in an *atonal*-associated nucleic acid sequence or amino acid sequence.

34. The method of claim 18, 19, 20, 21, 22, 23, 24, 25 or 26, wherein said amino acid sequence has at least about 80% identity to about 20 contiguous amino acid residues of SEQ ID NO:58 (Hath1).

15 35. The method of claim 18, 19, 20, 21, 22, 23, 24, 25 or 26, wherein said nucleic acid sequence encodes a polypeptide which has at least about 80% identity to about 20 contiguous amino acid residues of SEQ ID NO:58 (Hath1).

36. The method of claim 18, 19, 20, 21, 22, 23, 24, 25 or 26, wherein said cell is a human cell.

20 37. The method of claim 20 or 21, wherein said delivery comprises injecting into an inner ear a therapeutically effective amount of an *atonal*-associated amino acid sequence or nucleic acid sequence.

38. The method of claim 23 wherein said joint disease is osteoarthritis.
39. The method of claim 24 or 25, wherein said cell is a cancer cell.
40. A composition comprising an *atonal*-associated amino acid sequence or nucleic acid sequence in combination with a delivery vehicle, wherein said delivery vehicle results in delivery of a therapeutically effective amount of *atonal*-associated nucleic acid sequence or amino acid sequence into a cell.
41. The composition of claim 40, wherein said delivery vehicle comprises a vector that expresses an *atonal*-associated nucleic acid sequence or amino acid sequence in an animal cell.
42. The composition of claim 41, wherein said vector is selected from the group consisting of an adenoviral vector, a retroviral vector, an adeno-associated vector, a plasmid, a liposome, a protein, a lipid, a carbohydrate and a combination thereof of said vehicles.
43. The composition of claim 41, wherein said vector is selected from the group consisting of a viral vector or a non-viral vector.
44. The composition of claim 40, wherein said delivery vehicle is the receptor-binding domain of a bacterial toxin.
45. The composition of claim 40, wherein said *atonal*-associated nucleic acid sequence is operatively linked to nucleic acid sequence encoding a receptor-binding domain of a bacterial toxin.
46. The composition of claim 40 wherein said *atonal*-associated nucleic acid sequence is operatively linked to nucleic acid sequence encoding a protein transduction domain.

0990381.030600
0090381.030600

could
AI

47. A fusion protein comprising an *atonal*-associated amino acid sequence or fragment thereof and a desired amino acid sequence.
48. A nucleic acid sequence encoding the fusion protein of claim 47.
49. A method of delivering an *atonal*-associated amino acid sequence to an animal, wherein the method comprises administering to the animal a nucleic acid sequence encoding an *atonal*-associated amino acid sequence and a nucleic acid sequence encoding an additional therapeutic amino acid sequence.
50. The method of claim 20, wherein the method comprises delivering an *atonal*-associated nucleic acid sequence and a second nucleic acid sequence encoding a non-*atonal*-associated therapeutic agent.
51. The method of claim 21, wherein the method comprises delivering an *atonal*-associated nucleic acid sequence and a second nucleic acid sequence encoding a non-*atonal*-associated therapeutic agent.
52. The method of claim 22, wherein the method comprises delivering an *atonal*-associated nucleic acid sequence and a second nucleic acid sequence encoding a non-*atonal*-associated therapeutic agent.
53. The method of claim 24, wherein the method comprises delivering an *atonal*-associated nucleic acid sequence and a second nucleic acid sequence encoding a non-*atonal*-associated therapeutic agent.
54. The method of claim 26, wherein the method comprises delivering an *atonal*-associated nucleic acid sequence and a second nucleic acid sequence encoding a non-*atonal*-associated therapeutic agent.
55. The composition of claim 40, wherein the composition further comprises an additional amino acid sequence or nucleic acid sequence that is not an *atonal*-associated nucleic acid sequence or amino acid sequence.